REMARKS

Claims 1-7, 13-14, 16-17, 20-21, 23, 27-28 are now pending. Claims 1-7, 13-14, 16-17, 20-21, 23, 27-28 have been canceled without prejudice to or disclaimer of the subject matter therein. Former Claims 1-7, 13-14, 16-17, 20-21, 23, 27-28 have been replaced by new Claims 29-53. These claims derive support from throughout the Specification and claims originally filed. No new matter has been added.

CLAIM OBJECTIONS

Claims 1, 4, 7 and 20-21 have been objected to as purportedly having grammatical and typographical errors. Applicants disagree. Nevertheless, without conceding to the Examiner's objections, and only to expedite the prosecution of the subject application, Claims 1, 4, 7 and 20-21 have been replaced by new Claims 29, 34, 39 and 49-50, respectively. In light of these changes, withdrawal of this objection is requested.

Claim 23 has been objected to under 37 C.F.R. 1.75(c), as purportedly being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicants disagree. Nevertheless, without conceding to the Examiner's objections, and only to expedite the prosecution of the subject application, Claim 23 has been replaced by new claim 51 to recite a "cultured" plant as suggested by the Examiner. In light of the foregoing changes, withdrawal of this objection is requested.

CLAIM REJECTIONS: 35 U.S.C. § 112, FIRST PARAGRAPH

The Examiner has rejected Claims 1-2, 4-5, 7, 13-14, 16-17, 20-23 and 27-28 under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for nucleic acids of SEQ ID NO:2 and plant cells and plants transformed with those nucleic acids, allegedly does not reasonably provide enablement for nucleic acids that encode SEQ ID NO:1, encode modified nucleic acids or that hybridize under unspecified stringency to nucleic acids that encode SEQ ID NO:1.

Specifically, the Examiner alleges that undue experimentation is needed because the specification fails to provide guidance regarding which amino acids can be deleted or which regions of the protein can tolerate insertions to continue producing a functional enzyme. Applicants respectfully traverse this rejection.

MPEP § 2164 recites that the disclosure must "contain sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention. . ." without undue experimentation.

It is well within the purview of the skilled artisan and the teachings of the subject specification to modify nucleotide sequences by deletion, substitution or insertion and then determine if such modified sequences maintain the desired enzymatic activity. Further, it is well within the purview of the skilled artisan to produce modified nucleotide sequences and determine if such modified sequences hybridize to the sequence of SEQ ID NO:1 under stringent conditions. Furthermore, it is well within the purview of the skilled artisan to determine if proteins encoded by these modified nucleic acids maintain the recited enzymatic activities. These types of experimentation are merely routine and do not

constitute undue experimentation. Applicants direct the Examiner's attention to the specification Example 1-9. Example 1 illustrates the purification scheme used to purify the protein encoded by SEQ ID NO:2. The purified protein of Example 1 lacks the N-terminal amino acids of the original non-purified protein and is labeled SEQ ID NO:1. The truncated N-terminal of this protein is sequenced according to Example 2. This N-terminal contains 20 amino acids starting with "Phe" and is labeled SEQ ID NO:4. In the specification, at page 29, Table 1, clearly shows that SEQ ID NO:1 has an enzymatic activity identical to that of the non-purified protein encoded by SEQ ID NO:2. Applicants assert that it is routine in the art to develop a nucleotide sequence which encodes SEQ ID NO:1. Applicants direct the Examiner's attention to Examples 4-7 in which the specification illustrates the use of RT-PCR to isolate the coding sequence from a tea cDNA library. Transformation of bacteria using DNA sequences is well within the purview of a skilled artisan and routine in the art. The specification need not teach what is known in the art. In fact, the Federal Circuit has stated that a patent need not teach, and preferably omits, what is well known in the art. *See Hybritech, Inc. v. Monoclonal Antibodies, Ind.*, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986).

However, in order to expedite prosecution in the subject application, and not to acquiesce to the Examiner's rejection, Applicants have canceled rejected Claims 1-28 without disclaimer or prejudice and have added Claims 29-53. Claims 29 and 30 represent Claim 1 part (a) and (b), and 34 and 35 represent Claim 4 part (a) and (b), respectively. The specification, at pages 7-11, clearly discloses the method for making a modified SEQ ID NO:1, using hybridization under stringent conditions. Furthermore, new Claims 30 and

35 recite stringent hybridization conditions in detail, based on the specification pages 8-9. Undue experimentation is not required to practice the claimed invention.

Additionally, the Examiner notes that SEQ ID NO:1 does not appear to be the entire protein sequence. The Examiner alleges that "there is no evidence to suggest that a nucleic acid encoding only SEQ ID NO:1 would function to encode an enzyme with the listed properties, especially since the starting ATG is missing." Applicants respectfully disagree.

Applicants direct the Examiner's attention to the specification, Table 1, Examples 1-2 and Example 9. The results shown by these Examples clearly provide that"a nucleic acid encoding SEQ ID NO:1 functions to encode an enzyme with the listed properties," even with the starting ATG sequence missing. The specification at page 37, lines 16-19, states that by using the procedures disclosed in Example 9 the encoded isolated enzyme (SEQ ID NO:1) had the listed properties of three different N-methyl transferase activities.

Furthermore, Applicants direct the Examiner's attention to an article entitled "Purification and Characterization of Caffeine Synthase from Tea Leaves" (*Plant Physiology*, June 1999, Vol. 120, pp. 579-586). This article is co-authored by the named co-inventors of the subject application. This article discloses that the purified caffeine synthase described also has modified N-terminal parts (see page 584, Figure 5). This caffeine synthase also has the activity shown in Table 1 (see page 582). This article provides clear evidence that a truncated protein which is similar to SEQ ID NO:1 is fully active.

The Examiner further alleges that anti-sense suppression of genes is very unpredictable, therefore, it is not certain that such gene will inhibit sense gene transcription

or secondary metabolite levels when transformed into a plant of a different species. Furthermore, the Examiner alleges that the specification does not teach production of "ANY" plant metabolite, nor does it provide guidance for altering the "composition" of any plant metabolite.

Applicants submit that it is well within the purview of the skilled artisan and the teachings of the subject specification to make and use anti-sense suppression genes that are not completely homologous to the target gene which will inhibit sense gene transcription or secondary metabolite levels when transformed into a plant of a different species. Applicants direct the Examiner's attention to the specification, at page 25, regarding making and using sense or anti-sense DNA to obtain transformed plants for purpose of improving productivity for specific compounds by modifying the metabolism of such compound in the host plant.

Furthermore, Applicants direct the Examiner's attention to the specification, Example 10 - suppression of caffeine synthesis according to and anti-sense method; (page no.37). This Example illustrates the construction and use of a recombinant vector carrying an anti-sense N-methyl transferase gene which resulted in a significant reduction in production of the plant secondary metabolite, caffeine, in a caffeine producing plant. The specification discloses one method for making and using the claimed invention that bears reasonable correlation to the entire scope of the claim. Therefore, the enablement requirement of 35 U.S.C. § 112 is satisfied.

In re Fischer, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). "As long as the specification discloses at least one method for making and using the claimed invention that

bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. § 112 is satisfied."

Applicants further disagree with the Examiner that the instant specification relates to "ANY" plant metabolite. Applicants direct the Examiner's attention to the specification at page 25, second paragraph, for the definition of secondary metabolites. To prevent uncertainty or ambiguity Applicants, in the specification, have disclosed the compounds that "plant secondary metabolites" encompass by using Markush Groups. It is clearly stated that "a plant secondary metabolite is selected from a group consisting of 7-methyl xanthine, paraxanthine, theobromine, and caffeine." This means that Applicants have provided a clear definition of the term "a plant secondary metabolite" in the specification.

Applicant also disagree with the Examiner that instant specification provides no guidance for altering the "composition" of caffeine. In the newly added claims, the word "comprising" has been replaced by the word "concentration" as the Examiner had suggested. Therefore, this rejection as it pertains to the word "composition" is moot.

In light of the forgoing amendments and arguments, Applicants respectfully request the withdrawal of this rejection.

The Examiner has maintained his rejection of Claims 1-2, 4-5, 7, 13-14, 16-17, 20-23 and 27-28 under 35 U.S.C. § 112, first paragraph, as purportedly lacking a written description. The Examiner alleges that the specification "does not describe the structural features, i.e., the sequence, of nucleic acids that hybridize to a nucleic acid that encodes SEQ ID NO:1 and that encode a protein with" all three enzymatic activities. Based

thereon, the Examiner has concluded that "critical structural motifs that distinguish nucleic acids that encode functional enzymes from those that do not are not described."

In its decision in *In re Bell*, Federal Circuit stated that,

> "in the molecular biology arts, if an applicant disclosed an amino acid sequence, it would be unnecessary to provide an explicit disclosure of nucleic acid sequence that encoded the amino acid sequence. Since the genetic code is widely known, a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence. . . ."

Cf. In re Bell, 991 F.2d 781, 785 (Fed. Cir. 1993) and *In re Bell, 16 F.3d 380, 382 (Fed. Cir. 1994)*

Applicants respectfully submit that the subject specification teaches the amino acid sequence of SEQ ID NO:1. According to the decision of the Federal Circuit recited above, because genetic code is "*widely known*," it is "*unnecessary*" to disclose the nucleic acid sequence, *i.e.*, the structure of the nucleic acid, that encode the amino acid sequence of SEQ ID NO:1.

Therefore, Applicants submit that it is well within the purview of the skilled artisan to modify nucleotide sequences by deletion, substitution or insertion and then determine if such modified sequences maintain the desired enzymatic activity. Further, it is well within the purview of the skilled artisan to produce modified nucleotide sequences and determine if such modified sequences hybridize to the sequence of SEQ ID NO:1 under stringent conditions. Furthermore, it is well within the purview of the skilled artisan to determine if proteins encoded by these modified nucleic acids maintain the recited enzymatic activities. The specification need not teach what is known in the art. In fact, the Federal Circuit has

stated that a patent need not teach, and preferably omits, what is well known in the art. *See Hybritech, Inc. v. Monoclonal Antibodies, Ind.*, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986).

Furthermore, Applicants have replaced the rejected claims with new claims. Therefore, from the foregoing Applicants respectfully request the withdrawal of this rejection.

CLAIMS REJECTED UNDER U.S.C. § 112, SECOND PARAGRAPH

Claims 1-7, 13-14, 16-17, 20-21, 23 and 27-28 have been rejected under U.S.C. § 112, second paragraph, as purportedly indefinite.

Claims 1(b) and 4(b) have been rejected for allegedly lacking antecedent basis for "modified nucleic acid." Claims 1 and 4 have been cancel without prejudice or disclaimer. This rejection as it pertains to these canceled claims is respectively moot.

Claims 1(b) and 4(b) have been rejected as allegedly indefinite for recitation of phrase "stringent conditions." Claims 1 and 4 have been cancel without prejudice or disclaimer. This rejection as it pertains to these canceled claims is respectively moot.

Claims 2 and 5 are allegedly indefinite for recitation of "hybridized at a . . . to overnight." The Examiner alleges that because the "salt conditions are recited, nor are they unambiguously defined in the specification, the stringency of the conditions are unclear." Applicants submit that Claims 2 and 5 have been canceled without prejudice or disclaimer and replaced by new Claims 32 and 37. Claims 32 and 37 do not recite the salt conditions but they recite "hybridized under stringent conditions at a . . . to overnight." this rejection as it relates to Claims 2 and 5 is moot.

Claims 2 and 5 are allegedly indefinite in their recitation of "said nucleotide sequence (a) or said nucleotide sequence (b)." Claims 2 and 5 have been replaced by new Claims 32 and 37 which do not include the above language. This rejection as it relates to the canceled Claims 2 and 5 is moot.

Claims 3 and 6 are rejected as allegedly lacking antecedent basis for the limitation "said nucleotide sequence (a)." Claims 3 and 6 have been replaced by new Claims 33 and 38 which do not recite the above phrase. Thus this rejection as it pertains to the canceled Claims 3 and 6 is moot.

Claim 7 has been rejected as indefinite. Claim 7 has been replaced by new Claim 39. This rejection as it relates to canceled Claim 7 is moot.

Claim 20 allegedly lacks antecedent basis for the limitation "the transformed . . . whole plant" in line 3. Claim 20 has been replaced by new Claim 49. This rejection as it pertains to canceled Claim 20 is moot.

Claim 21 is allegedly indefinite because it lacks agreement between the preamble of the methods that the positive method steps. Claim 21 has been deleted, thus rendering this rejection moot.

CONCLUSION

Prompt issuance of a Notice of Allowance is earnestly solicited. In the event any questions arise regarding this communication or the application in general, please contact Applicant' undersigned representative at the telephone number listed below.

Respectfully submitted,

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